

**Challenges and inequalities of opportunities in European psychiatry research:
The example of psychodiagnostic tool availability in
research on early autism identification**

Sven Bölte^{1,2}, Przemyslaw Tomalski³, Peter B. Marschik^{1,4}, Steve Berggren^{1,2},
Joakim Norberg¹, Terje Falck-Ytter^{1,5}, Olga Pokorska³, Emily JH Jones⁶,
Tony Charman⁷, Herbert Roeyers⁸, Elzbieta Kostrzewa¹ and
members of the COST action ESSEA BM1004 work groups*

¹Center of Neurodevelopmental Disorders (KIND), Department of Women's and
Children's Health, Karolinska Institutet, Stockholm, Sweden

²Division of Child and Adolescent Psychiatry, Stockholm County Council, Sweden

³Neurocognitive Development Lab, Faculty of Psychology, University of Warsaw, Poland

⁴Institute of Physiology, Center for Physiological Medicine,
Medical University of Graz, Austria

⁵Uppsala Child and Babylab, Department of Psychology, Uppsala University, Sweden

⁶Centre for Brain and Cognitive Development, Birkbeck College, University of London, UK

⁷Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK

⁸Department of Experimental Clinical and Health Psychology, Ghent University, Belgium

*see acknowledgement for names and affiliations

Corresponding author: Professor Sven Bölte, Center of Neurodevelopmental Disorders

(KIND), Neuropsychiatry Unit, Department of Women's and Children's Health, Karolinska

Institutet, Sweden; sven.bolte@ki.se; CAP Research Center, Gävlegatan 22,

11330 Stockholm, Sweden

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Summary

Background: Europe is diverse in terms of economy, cultures, socio-demography and languages. A crucial aspect of psychiatric research is the availability of standardized screening, diagnostic and characterization instruments. Aims/Method: We fine-mapped the accessibility of 14 clinical scales and cognitive tests **for the assessment of** early childhood autism spectrum disorder [ASD] (e.g. ADOS, ADI-R, SCQ, SRS, CHAT, MESL) within 21 European countries. These tools are essential for internationally competitive early ASD **detection** research. Results: We identified a considerable variation not only in the availability, but also psychometric standardization, and formal distribution of the instruments between the countries, privileging English speaking, high-income and highly populated European countries. Absence of country-specific standardization was a problem across many countries, independent of income and size. Discussion: Findings demonstrate, on a concrete level, the challenges in creating equal early ASD **identification** research opportunities in Europe, and the need for increased funding for instrument development and validation. We discuss the reasons, implications and consequences of this inequity and ways of reducing it.

Key Words: Assessment, neurodevelopmental disorders, mental health, tests, psychometrics

Introduction

Europe is diverse in terms of cultures and languages, comprising 53 countries according to the WHO definition (including parts of geographical Asia), of which 28 are currently organized under the European Union (EU). Although many European countries are developed high-income countries, this should not camouflage the huge differences between high and less developed countries. For instance, following the World Bank's (worldbank.org) 2013/14 classification of low and middle income (LAMI) countries, a noteworthy number of 17 European countries are still judged as low-middle (e.g. Albania, Georgia, Moldova, Ukraine) or upper-middle income (e.g. Bulgaria, FYR Macedonia, Romania, Turkey), of which 4 are EU countries. Clinical and research psychiatry is equally diverse across Europe, with substantial variations even within countries due to federalism or regionalization (Evans-Lacko et al., 2014; Muijen, 2012). As for the world-wide situation, research output in Europe is dominated by the high-income countries (Muijen, 2012; Sumathipala et al., 2004).

ASD is a neurodevelopmental condition defined by overarching impairments in the areas of reciprocal social communication and interaction, alongside a preference for repetitive, stereotyped activities, patterns of behaviors and interests (Bölte & Hallmayer, 2011). ASD has emerged a top priority health care issue in many countries (see for instance USA: "Combating Autism Act of 2006", "Autism Treatment Acceleration ACT of 2009"; or UK: Autism Act UK, 2009) because of increasing rates of diagnoses (in high income countries) around the globe (Elsabbagh et al., 2012), as well as high associated societal challenges and costs (Gustavsson et al., 2011) of educational and clinical care. In recent years, a growing interest in early detection of ASD has emerged, mostly driven by the insight that early identification is a prerequisite for early intervention, which itself may improve long-term outcomes for individuals with ASD (Dawson, 2008). Several methodologies have helped to investigate early detection and intervention in ASD, in particular screening studies and

research on high-risk siblings (Bölte et al., 2013; Garcia-Primo et al., 2014; Ozonoff et al., 2011).

The availability of standardized diagnostic instruments is a crucial prerequisite for conducting high-quality early ASD **detection** research. Without evidence-based standardized phenotyping in psychiatry there is a risk of diagnostic bias and “garbage in, garbage out” research. Significant progress has been made over the past two decades in the development of reliable and valid phenotyping tools for ASD (Charman & Gotham, 2013). Many of these instruments are part of national or regional clinical guidelines for ASD in European countries (Arngrim et al., 2013; "Autism diagnosis in children and young people. Recognition, referral and diagnosis of children and young people on the autism spectrum,"), while some are viewed as a “gold standard”, most notably the Autism Diagnostic Observation Schedule, Second Edition (Hus, Gotham, & Lord, 2012) combined with the Autism Diagnostic Interview-Revised (Rutter, Le Couteur, & Lord, 2003). Publication of ASD research findings in leading ASD or general psychiatry journals can be challenging or even impossible without these tools. Nevertheless, their availability, validation and standardization are limited to a small group of languages and cultures. The latter substantially limits international collaboration, and research opportunities for many countries, even in Europe, perhaps particularly for the LAMI countries among them.

The goal of this study was to inventory the accessibility and standardization of diagnostic instruments for early identification of autism across 21 European countries.

Instruments were mapped that are currently required for internationally competitive early ASD identification research. With this work we aim to highlight potential challenges and (in-)equalities of science opportunities across Europe in a concrete manner. The findings might be valuable to further raise awareness of research barriers in Europe and beyond, and to direct the focus of international public policy on these issues. This is particularly important for

LAMI countries, but also for less populated countries and those with less commonly spoken languages.

Methods

Participants and procedure

The study was carried-out between November 2013 and April 2014. Twenty-one European countries involved in the COST (European Cooperation in Science and Technology; www.cost.eu) action “Enhancing the Scientific Study of Early Autism” (ESSEA; for details see www.cost-essea.com) participated. COST-ESSEA is a network of over 60 scientists from 23 European countries, including three LAMI countries (Romania, FYR Macedonia, and Turkey), intending to develop capacity in early autism research across all action members.

The principal investigators or research groups’ contact persons for each of the COST ESSEA research network countries were surveyed. They were the official COST ESSEA management committee representatives for their countries¹, chosen by the chair, vice chair and the four working group leaders of the action based when a country entered the network based on documented scientific experience and excellence in the area of early ASD **assessment research**. The countries were partly clustered for the study to form 16 language/cultural groups that in practice usually use the same versions of adapted diagnostic tools:

Austria/Germany/Switzerland (German), Belgium/The Netherlands (Dutch), Czech Republic, Finland, France (including information on French-Canadian adaptations of tools), Hungary, Iceland, Italy, Israel, Macedonia, Poland, Portugal (including information on Brazilian adaptations of tools), Spain, Sweden/Norway (Scandinavia), Romania, and UK/Ireland (English; even US-versions of instruments included here). Excel spreadsheet inventories containing items about the availability and standardization of language/culturally adapted

¹ See: https://e-services.cost.eu/w3/index.php?id=1627&action_number=BM1004

versions of diagnostic instruments often used in leading research on early ASD identification were generated. They included 4 items: (1) Existence of domestic (language) versions of the instruments, (2) Domestic psychometric data (norms, reliability, validity) published, (3) Copyright for the instrument, (4) Published studies, on each of the 14 scales/tests (see section “inventoried instruments” below). The spreadsheets were sent via e-mail to the principal investigators or research groups’ contact persons and returned electronically. The returned material was analyzed, missing or inconsistent data was added or corrected by the authors based on own knowledge, searches in existing databases (e.g. Pubmed, PsychInfo), correspondence with publishers as well the original authors of the mapped diagnostic tools, and summarized to form an overview on the availability of the clinical scales and psychological tests across the 16 language/cultural groups. Finally, the overview was sent to the informants for approval. Before submission (December 2014) of this article some information was updated to include the most recent developments.

The selection of early ASD diagnostic instruments was based on a research protocol developed within “European Autism Interventions - A Multicentre Study for Developing New Medications (EU-AIMS; www.eu-aims.eu). Herein, and using Delphi method, leading European labs of ASD research have agreed on a common protocol of 14 clinical scales and psychological tests currently deemed the most adequate ones for research on early ASD detection, owing to their scientific quality, as well as scientific and clinical usage from an international perspective. An overview of this shared protocol is available online (www.eurosibs.eu), and the strategic concepts of EU-AIMS in terms of assessments and patient characterization are described elsewhere in detail (Ashwood, Buitelaar, Murphy, Spooren, & Charman, 2014). The instruments are briefly introduced in the following section.

Inventoried instruments

ASD-specific scales. (1) The Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) is a play and interview-based observation scale administered by experienced and specifically trained clinicians operationalizing DSM-IV/DSM-5 criteria for ASD in an empirically derived diagnostic algorithm. Different modules of the instrument are applied depending on the individual's age and expressive language level. Module T (for toddlers; no speech to single phrases, age 12-30 months) and module 1 (no speech to single phrases, >31 months of age to school age) are most relevant to **early ASD assessment research**; (2) The Autism Diagnostic Interview-Revised (ADI-R) is an investigator-based structured diagnostic caregiver interview, also operationalizing DSM-IV/DSM-5 criteria for ASD in a diagnostic algorithm. It can be used for individuals with suspected ASD of any age, although it is preferably used for children and adolescents. Recently, specific ADI-R diagnostic algorithms for toddlers and preschoolers have been published (Kim, Thurm, Shumway, & Lord, 2013). The combined use of the ADI-R and ADOS is often viewed as the first choice of diagnosing ASD in research and practice. This is true even for early ASD assessments (Zander, Sturm, & Bölte, 2014); (3) The Social Communication Questionnaire (SCQ) is a parent-report clinical ASD screener derived from the ADI-R. There are two versions: the "current" and the "lifetime" version; (4) The Social Responsiveness Scale (SRS) is a parent or teacher report questionnaire of autism traits for children aged 4-18 years. The preschool version of the SRS (SRS-P) covers the age range of 3 to 4 years; (5) The Development and Well-Being Assessment (DAWBA) is a group of interviews, questionnaires and rating scales to enable ICD-10/DSM-IV psychiatric diagnoses on 5-17 year olds; DAWBA results can be inserted into a computer program algorithm that generates probabilities for a range of psychiatric disorders, including ASD. The provisional computer-generated diagnoses are then reviewed by an expert clinician; (6) The Quantitative (Q)-CHAT

and the Modified (M)-CHAT/-Revised are early parent-report ASD screeners for young children aged between 16/18 to 24/30 months of age; (7) The Repetitive Behavior Scale (RBS) is a questionnaire that captures the breadth of stereotypic behaviors in individuals of any age with ASD on five dimensions, namely ritualistic/sameness behavior, stereotypic behavior, self-injurious behavior, compulsive behavior, and restricted interests. For comprehensive references see “Supplementary Materials”.

Non ASD-specific psychological tests and clinical scales. (8) The MacArthur-Bates Communicative Development Inventory (CDI) is a parent-/caregiver report tool for assessing language and communication development in infants and children. In most versions, it comes in two scales, an infant (8 to 16 months), and a toddler scale (16 to 30 months), capturing comprehension, word production and aspects of symbolic and communicative gesture, word production and the early grammar. Short screening version exists for English and Spanish and several other languages; (9) The Mullen Scales of Early Learning is a clinician administered child development test to measure gross and fine motor, visual reception, and expressive and receptive language from birth to 68 months of age; (10) The Vineland Adaptive Behavior Scales (VABS) is a parent/caregiver report measure (administered as either a questionnaire or a clinical interview) of adaptive function in everyday life regarding social, communicative, daily living and motor skills (up to 6 years) from birth onwards; (11) The Infant-Toddler Sensory Profile (ITSP) is a parent/caregiver questionnaire on sensory processing patterns in infants (0-6 months) and toddlers (7-36 months), quantifying five domains: auditory, visual, tactile, vestibular, and oral sensory processing; (12) The Infant Behavior Questionnaire-Revised (IBQ-R) is a parent rated measure of infant temperament (3-12 months) on 14 subscales (e.g. activity level, distress to limitations, fear, smiling/laughter, cuddliness). Short and very short versions exist; (13) The Early Childhood Behavior Questionnaire (ECBQ) serves the same purpose as the IBQ-R, but in young children aged 18 and 36 months. It

ECBQ assesses 18 dimensions of temperament (e.g. attentional focus, cuddliness, discomfort, frustration, impulsivity, shyness); (14) The Child Behavior Checklist (CBCL) 1½ -5 is an assessment of general problem behaviors in preschool children. The information is obtained from parents or teachers using items on eight syndrome scales (emotionally reactive; anxious/depressed; somatic complaints; withdrawn; sleep problems, attention problems; rule-breaking behavior; aggressive behavior). For comprehensive references see “Supplementary Materials”.

Results

A detailed description of adaptations available for each of the reviewed scales or tests per country / linguistic region is provided in the supplementary tables and references (Suppl. Tables 1-14 & references): ADOS in Supplementary Table 1, ADI-R in Supplementary Table 2, SCQ in Supplementary Table 3, SRS in Supplementary Table 4, DAWBA in Supplementary Table 5, Q-CHAT and M-CHAT/-R in Supplementary Table 6, RBS-R in Supplementary Table 7, CDI in Supplementary Table 8, Mullen Scales of Early Learning in Supplementary Table 9, VABS in Supplementary Table 10, ITSP in Supplementary Table 11, IBQ-R in Supplementary Table 12, ECBQ in Supplementary Table 13, and CBCL 1½ -5 in Supplementary Table 14.

A substantial variation was identified in the availability of diagnostic instruments for different countries, cultures, or languages (Table 1), with only three regions (UK/Ireland, Scandinavia, and Belgium/The Netherlands) having access to sufficiently usable forms of all of the 14 diagnostic instruments. Additionally, clinicians and researchers from Israel and Portugal have access to 13 out of 14 proposed diagnostic instruments. For four of the surveyed countries (Romania, Hungary, FYR Macedonia and Czech Republic) less than half of the instruments have been translated or adapted.

About here: Table 1

Not surprisingly, the number of instruments being available per country from a commercial publisher or directly from the authors of the respective tool in an organized fashion (e.g. download from a website) (here called ‘formal distribution’) also varied for different languages and countries/regions. In addition, although many of the available diagnostic tools are also distributed formally, in most cases, the number of available tools is higher than the number of tools distributed formally. The exceptions are UK/Ireland, German speaking countries (Germany, Austria, and Switzerland), Spain, Iceland, and Romania in which all available tools are even distributed formally.

Generally, many of the available (and published) diagnostic instruments have not been specifically standardized for the different European languages and countries/regions (Table 1). Even in the regions with high availability of diagnostic instruments, country/language specific reliability and validity properties or norms/cut-offs are sparse (e.g. in France, Italy, Spain) or missing (e.g. in Israel, Portugal, Finland). German and English speaking countries are exceptions from this observation, even though in the UK and Ireland for some tools there is a high reliance on generalizability of studies from the USA. If one assumes generalizability across English speaking countries, the USA, UK, and Ireland are characterized by the highest number of available, formally distributed as well as normalized methods. Dutch speaking countries as well as Scandinavian countries are other examples of regions with relatively high availability of some usable forms of the diagnostic instruments, which are mostly formally distributed. Country/language specific normalization is, however, less common in case of these regions. Scientists and clinicians from German speaking countries can formally access 11 of the proposed diagnostic instruments, for which two thirds have a culture/language specific standardization. In the case of other regions, even if translated diagnostic instruments

are (formally or informally) available, specific standardizations are lacking. Clinicians and scientists from Czech Republic have the most limited access to diagnostic tools for early ASD assessment. Only 4 out of 14 tools have been translated to Czech, out of which two are formally available but none language specific data has been collected.

About here: Table 2

Table 2 shows the availability of each of the early ASD diagnostic instruments within the totality of European languages/cultural regions. The only widely available tool across Europe is the ADOS/ADOS-2, which is accessible across all the examined language/culture regions. The ADI-R, CBCL, M-CHAT/Q-CHAT and SCQ are available in the majority of regions. Nevertheless, there are not very many publications on these relatively well accessible methods originating in Europe (see Suppl Tables 1-14 & references). Two instruments are particularly infrequently available in Europe: The Mullen Scales of Early Learning and the RBS-R (both available in 4 languages/culture regions). Among the formally distributed tools available in different language versions from commercial publishers are the ADOS-2 and ADI-R. The process of getting both of these published is protracted and takes several years. Instruments formally distributed by their authors are the DAWBA, M-CHAT, and MacArthur-Bates Communicative Development Inventory. Instruments with poor distribution are the ITSP, RBS-R and Mullen Scales of Early Learning. Region/language specific standardizations are scarce or missing for many of the early ASD diagnostic instruments. This holds true even for tools with greater availability. The CDI can be partially considered an exception because it is available in 13 out of 16 examined regions and it has specific norms for 7 of the countries.

Discussion

Psychiatric research is based on reliable phenotyping, predominantly ensured by psychodiagnostic tools including first choice diagnostic instruments (“gold standard”) to determine psychiatric status, general psychopathology or psychological characteristics (e.g. neuropsychological functions, IQ). Nevertheless, many of these scales and tests are only available in a limited number of languages, and have been normalized and validated for an even smaller number of cultural backgrounds. This study examined the (in-)equalities of research prerequisites across Europe regarding the access to diagnostic instruments enabling internationally competitive **research on early ASD identification**. Our study suggests that the middle-income countries are disadvantaged in Europe. The two included middle-income European countries (Romania, FYR Macedonia) had limited access to diagnostic scales compared to high-income European countries. In addition, limited access to certain instruments was identified in other east European countries (Czech Republic, Hungary, Poland) as well as Iceland, a country with a small population and its own language. However, even in these countries the access to a smaller selection of ASD specific scales, such as the ADOS-2, ADI-R, SCQ or M-CHAT/Q-CHAT or instruments used frequently in international research and practice to evaluate general psychopathology (CBCL) was satisfactory. These scales are either formally distributed by commercial publishers or freely and systematically made available by the authors. A further, less recognized issue in this context is the level of availability of each instrument to clinicians as well the availability of adequate clinical and research training. In many countries where certain tools are not formally distributed, they have been adapted for research purposes only. This means that each administration is subject to license fees paid directly to the copyright holder and in result the instrument is not available for clinical practice. Thus tool availability is further impounded by the need to negotiate license agreements with the publisher of the original version, while the publisher

often sets a number of limitations on the use of data collected with this instrument. This is a particularly sensitive issue in the face of increasing demands for free access to research data put forward by public research funding bodies. As the purpose of this mapping was to examine if European countries can adhere to internationally competitive research protocols (www.eu-aims.eu; www.eurosibs.eu), not the usage of ASD diagnostics in European clinical practice, we did not examine frequencies of usage of the various instruments in relation to either commercial or free distribution. We are therefore unable to evaluate which of the two is generally more beneficial for accessibility and usage. The latter is surely a limitation of the current study, and deserves more attention in future research. It is of paramount interest to the EU-AIMS project mentioned earlier, and strategies and actions to solve related obstacles in Europe have been recently described (Ashwood, Buitelaar, Murphy, Spooren, & Charman, 2014). Still, as commercially distributed instruments are associated with costs for purchase, which are often high for LAMI countries, and entail stricter rules for copyright and terms of usage, free access is probably more advisable to reduce inequalities of research prerequisites concerning instrument access. However, even free access might not solve other challenges for LAMI countries, such as limited access to (expensive) training to ensure quality control of administration, scoring and interpretation, like currently required for the ADOS-2 and ADI-R.

Strikingly, we found that for all European languages/cultural regions, no matter high or middle income, small or large population and rare or frequently spoken language, there was a substantial deficiency of adequate language/cultural standardization. The only language for which standardization was sufficient across instruments was English (UK/Ireland), but only when assuming high intercultural validity between these countries and USA. Most scales originate from the USA, and generalizability of psychometric properties and norms to high income European countries is often assumed. However, several studies, for instance those from Germany or Sweden on the ADOS-2, ADI-R or SRS show that this is only partially true

(Bölte & Poustka, 2004; Bölte, Poustka, & Constantino, 2008; Zander et al., 2014). The latter demonstrates the need for increased cross-cultural research in the field of psychometric evaluation, an extremely and continuously underfunded area of science. This is unfortunate, as a large part of psychiatric research of all kind is based on reliable phenotyping, predominantly ensured by psychodiagnostic tools.

Reasons for international research imbalances in terms of tool availability and other aspects are multifaceted. Proximal causes include the fact that the amount of research conducted in LAMI countries is comparably small and more likely to be of lower scientific quality than in high-income countries (Alem & Kebede, 2003). There are extremely few research skilled psychiatrists, clinical psychologists and other mental health professionals, and those who are, mostly work clinically, with a strong need to focus on health care services. Researchers face difficult circumstances in LAMI countries, owing to social, political and economic situations that do not or cannot prioritize psychiatry research, leading to a lack of funding, poor equipment, and inadequate education. Moreover, a low level of scientific culture with no research and publication tradition hampers research (Jablensky, 1999). Our study also points out research disadvantages in developed countries with small populations and rarely spoken languages (e.g. Iceland). This is an obvious challenge, but it has rarely been discussed previously in the literature.

The underrepresentation of certain countries, especially LAMI countries in psychiatry research is both ethically and scientifically challenging. Ethically, The World Mental Health report has pointed-out the immense burden of psychiatric problems and disability that are associated with mental disorders in LAMI countries (Desjarlais, 1996), and the research gap also reflects the well-known 10/90 global divide: less than 10% of the world's research resources are earmarked for more than 90% of the health problems (*The 10/90 report on health research 2000*). Scientifically, it is reasonable to support the use of the research

capacities and findings from LAMI countries. Their inclusion might reduce research and publication bias, by providing a lot broader perspective on mental health and possibly new significant insights into basic and applied psychiatry. To a lesser degree this might even be true for developed countries, with small populations or rarely spoken languages.

To increase underrepresented countries, collaborative research between LAMI and more scientifically established countries is fruitful (Doku & Mallett, 2003). Several international collaborations have previously raised awareness for inequalities in psychological and psychiatric research prerequisites including the availability of scales to assess child development. For instance, The World Psychiatric Association (WPA) Task Force, initiated activities aiming to support psychiatry journals (e.g. with PubMed indexation) in LAMI countries (de Jesus Mari et al., 2009), the Grand Challenges in Global Mental Health initiative by the US National Institute of Mental Health has identified research priorities to impact on mental health internationally (Collins et al., 2011), The WHO-launched collaborative longitudinal study of schizophrenia (Padma, 2014), and the Grand Challenges in Global Mental Health initiatives (Collins et al., 2011) aim to disclose overseen obstacles for international psychiatric research. In terms of diagnostic tool availability, The Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) cohort study (Murray-Kolb et al., 2014). Across 8 sites, in Bangladesh, Brazil, India, Nepal, Pakistan, Peru, South Africa, and Tanzania, the Bayley Scales of Infant and Toddler Development and a modified MacArthur Communicative Development Inventory were adapted. Herein, the authors explicitly point-out the complexity and costs of worldwide psychodiagnostic tool harmonization, in order to raise awareness among funders for future research support in this area of science.

The current mapping study is the first to review lacking diagnostic scale availability in **early assessment** of childhood ASD for research purposes from a cross-national perspective.

Initiatives such as COST-ESSEA, and outcomes from these initiatives, such as the present study, can help to generate awareness of research inequalities in ASD and other neurodevelopmental disorders. They might serve as a decision pad for policy makers and the international research community to overcome those inequalities. Future studies in the area should investigate the status quo of tool availability in ASD beyond Europe, also include scales for adolescent and adult ASD, and also incorporate research prerequisites in relation clinical practice.

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Challenges and inequalities of opportunities in European psychiatry research:

The example of psychodiagnostic tool availability in research on early autism identification

Summary

Background: Europe is diverse in terms of economy, cultures, socio-demography and languages. A crucial aspect of psychiatric research is the availability of standardized screening, diagnostic and characterization instruments. Aims/Method: We fine-mapped the accessibility of 14 clinical scales and cognitive tests for the assessment of early childhood autism spectrum disorder [ASD] (e.g. ADOS, ADI-R, SCQ, SRS, CHAT, MESL) within 21 European countries. These tools are essential for internationally competitive early ASD detection research. Results: We identified a considerable variation not only in the availability, but also psychometric standardization, and formal distribution of the instruments between the countries, privileging English speaking, high-income and highly populated European countries. Absence of country-specific standardization was a problem across many countries, independent of income and size. Discussion: Findings demonstrate, on a concrete level, the challenges in creating equal early ASD identification research opportunities in Europe, and the need for increased funding for instrument development and validation. We discuss the reasons, implications and consequences of this inequity and ways of reducing it.

Key Words: Assessment, neurodevelopmental disorders, mental health, tests, psychometrics

Introduction

Europe is diverse in terms of cultures and languages, comprising 53 countries according to the WHO definition (including parts of geographical Asia), of which 28 are currently organized under the European Union (EU). Although many European countries are developed high-income countries, this should not camouflage the huge differences between high and less developed countries. For instance, following the World Bank's (worldbank.org) 2013/14 classification of low and middle income (LAMI) countries, a noteworthy number of 17 European countries are still judged as low-middle (e.g. Albania, Georgia, Moldova, Ukraine) or upper-middle income (e.g. Bulgaria, FYR Macedonia, Romania, Turkey), of which 4 are EU countries. Clinical and research psychiatry is equally diverse across Europe, with substantial variations even within countries due to federalism or regionalization (Evans-Lacko et al., 2014; Muijen, 2012). As for the world-wide situation, research output in Europe is dominated by the high-income countries (Muijen, 2012; Sumathipala et al., 2004).

ASD is a neurodevelopmental condition defined by overarching impairments in the areas of reciprocal social communication and interaction, alongside a preference for repetitive, stereotyped activities, patterns of behaviors and interests (Bölte & Hallmayer, 2011). ASD has emerged a top priority health care issue in many countries (see for instance USA: "Combating Autism Act of 2006", "Autism Treatment Acceleration ACT of 2009"; or UK: Autism Act UK, 2009) because of increasing rates of diagnoses (in high income countries) around the globe (Elsabbagh et al., 2012), as well as high associated societal challenges and costs (Gustavsson et al., 2011) of educational and clinical care. In recent years, a growing interest in early detection of ASD has emerged, mostly driven by the insight that early identification is a prerequisite for early intervention, which itself may improve long-term outcomes for individuals with ASD (Dawson, 2008). Several methodologies have helped to investigate early detection and intervention in ASD, in particular screening studies and

research on high-risk siblings (Bölte et al., 2013; Garcia-Primo et al., 2014; Ozonoff et al., 2011).

The availability of standardized diagnostic instruments is a crucial prerequisite for conducting high-quality early ASD detection research. Without evidence-based standardized phenotyping in psychiatry there is a risk of diagnostic bias and “garbage in, garbage out” research. Significant progress has been made over the past two decades in the development of reliable and valid phenotyping tools for ASD (Charman & Gotham, 2013). Many of these instruments are part of national or regional clinical guidelines for ASD in European countries (Arngrim et al., 2013; "Autism diagnosis in children and young people. Recognition, referral and diagnosis of children and young people on the autism spectrum,"), while some are viewed as a “gold standard”, most notably the Autism Diagnostic Observation Schedule, Second Edition (Hus, Gotham, & Lord, 2012) combined with the Autism Diagnostic Interview-Revised (Rutter, Le Couteur, & Lord, 2003). Publication of ASD research findings in leading ASD or general psychiatry journals can be challenging or even impossible without these tools. Nevertheless, their availability, validation and standardization are limited to a small group of languages and cultures. The latter substantially limits international collaboration, and research opportunities for many countries, even in Europe, perhaps particularly for the LAMI countries among them.

The goal of this study was to inventory the accessibility and standardization of diagnostic instruments for early identification of autism across 21 European countries. Instruments were mapped that are currently required for internationally competitive early ASD identification research. With this work we aim to highlight potential challenges and (in-)equalities of science opportunities across Europe in a concrete manner. The findings might be valuable to further raise awareness of research barriers in Europe and beyond, and to direct the focus of international public policy on these issues. This is particularly important for

LAMI countries, but also for less populated countries and those with less commonly spoken languages.

Methods

Participants and procedure

The study was carried-out between November 2013 and April 2014. Twenty-one European countries involved in the COST (European Cooperation in Science and Technology; www.cost.eu) action “Enhancing the Scientific Study of Early Autism” (ESSEA; for details see www.cost-essea.com) participated. COST-ESSEA is a network of over 60 scientists from 23 European countries, including three LAMI countries (Romania, FYR Macedonia, and Turkey), intending to develop capacity in early autism research across all action members. The principal investigators or research groups’ contact persons for each of the COST ESSEA research network countries were surveyed. They were the official COST ESSEA management committee representatives for their countries¹, chosen by the chair, vice chair and the four working group leaders of the action based when a country entered the network based on documented scientific experience and excellence in the area of early ASD assessment research. The countries were partly clustered for the study to form 16 language/cultural groups that in practice usually use the same versions of adapted diagnostic tools: Austria/Germany/Switzerland (German), Belgium/The Netherlands (Dutch), Czech Republic, Finland, France (including information on French-Canadian adaptations of tools), Hungary, Iceland, Italy, Israel, Macedonia, Poland, Portugal (including information on Brazilian adaptations of tools), Spain, Sweden/Norway (Scandinavia), Romania, and UK/Ireland (English; even US-versions of instruments included here). Excel spreadsheet inventories containing items about the availability and standardization of language/culturally adapted

¹ See: https://e-services.cost.eu/w3/index.php?id=1627&action_number=BM1004

versions of diagnostic instruments often used in leading research on early ASD identification were generated. They included 4 items: (1) Existence of domestic (language) versions of the instruments, (2) Domestic psychometric data (norms, reliability, validity) published, (3) Copyright for the instrument, (4) Published studies, on each of the 14 scales/tests (see section “inventoried instruments” below). The spreadsheets were sent via e-mail to the principal investigators or research groups’ contact persons and returned electronically. The returned material was analyzed, missing or inconsistent data was added or corrected by the authors based on own knowledge, searches in existing databases (e.g. Pubmed, PsychInfo), correspondence with publishers as well the original authors of the mapped diagnostic tools, and summarized to form an overview on the availability of the clinical scales and psychological tests across the 16 language/cultural groups. Finally, the overview was sent to the informants for approval. Before submission (December 2014) of this article some information was updated to include the most recent developments.

The selection of early ASD diagnostic instruments was based on a research protocol developed within “European Autism Interventions - A Multicentre Study for Developing New Medications (EU-AIMS; www.eu-aims.eu). Herein, and using Delphi method, leading European labs of ASD research have agreed on a common protocol of 14 clinical scales and psychological tests currently deemed the most adequate ones for research on early ASD detection, owing to their scientific quality, as well as scientific and clinical usage from an international perspective. An overview of this shared protocol is available online (www.eurosibs.eu), and the strategic concepts of EU-AIMS in terms of assessments and patient characterization are described elsewhere in detail (Ashwood, Buitelaar, Murphy, Spooren, & Charman, 2014). The instruments are briefly introduced in the following section.

Inventoried instruments

ASD-specific scales. (1) The Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) is a play and interview-based observation scale administered by experienced and specifically trained clinicians operationalizing DSM-IV/DSM-5 criteria for ASD in an empirically derived diagnostic algorithm. Different modules of the instrument are applied depending on the individual's age and expressive language level. Module T (for toddlers; no speech to single phrases, age 12-30 months) and module 1 (no speech to single phrases, >31 months of age to school age) are most relevant to early ASD assessment research; (2) The Autism Diagnostic Interview-Revised (ADI-R) is an investigator-based structured diagnostic caregiver interview, also operationalizing DSM-IV/DSM-5 criteria for ASD in a diagnostic algorithm. It can be used for individuals with suspected ASD of any age, although it is preferably used for children and adolescents. Recently, specific ADI-R diagnostic algorithms for toddlers and preschoolers have been published (Kim, Thurm, Shumway, & Lord, 2013). The combined use of the ADI-R and ADOS is often viewed as the first choice of diagnosing ASD in research and practice. This is true even for early ASD assessments (Zander, Sturm, & Bölte, 2014); (3) The Social Communication Questionnaire (SCQ) is a parent-report clinical ASD screener derived from the ADI-R. There are two versions: the "current" and the "lifetime" version; (4) The Social Responsiveness Scale (SRS) is a parent or teacher report questionnaire of autism traits for children aged 4-18 years. The preschool version of the SRS (SRS-P) covers the age range of 3 to 4 years; (5) The Development and Well-Being Assessment (DAWBA) is a group of interviews, questionnaires and rating scales to enable ICD-10/DSM-IV psychiatric diagnoses on 5-17 year olds; DAWBA results can be inserted into a computer program algorithm that generates probabilities for a range of psychiatric disorders, including ASD. The provisional computer-generated diagnoses are then reviewed by an expert clinician; (6) The Quantitative (Q)-CHAT

and the Modified (M)-CHAT/-Revised are early parent-report ASD screeners for young children aged between 16/18 to 24/30 months of age; (7) The Repetitive Behavior Scale (RBS) is a questionnaire that captures the breadth of stereotypic behaviors in individuals of any age with ASD on five dimensions, namely ritualistic/sameness behavior, stereotypic behavior, self-injurious behavior, compulsive behavior, and restricted interests. For comprehensive references see “Supplementary Materials”.

Non ASD-specific psychological tests and clinical scales. (8) The MacArthur-Bates Communicative Development Inventory (CDI) is a parent-/caregiver report tool for assessing language and communication development in infants and children. In most versions, it comes in two scales, an infant (8 to 16 months), and a toddler scale (16 to 30 months), capturing comprehension, word production and aspects of symbolic and communicative gesture, word production and the early grammar. Short screening version exists for English and Spanish and several other languages; (9) The Mullen Scales of Early Learning is a clinician administered child development test to measure gross and fine motor, visual reception, and expressive and receptive language from birth to 68 months of age; (10) The Vineland Adaptive Behavior Scales (VABS) is a parent/caregiver report measure (administered as either a questionnaire or a clinical interview) of adaptive function in everyday life regarding social, communicative, daily living and motor skills (up to 6 years) from birth onwards; (11) The Infant-Toddler Sensory Profile (ITSP) is a parent/caregiver questionnaire on sensory processing patterns in infants (0-6 months) and toddlers (7-36 months), quantifying five domains: auditory, visual, tactile, vestibular, and oral sensory processing; (12) The Infant Behavior Questionnaire-Revised (IBQ-R) is a parent rated measure of infant temperament (3-12 months) on 14 subscales (e.g. activity level, distress to limitations, fear, smiling/laughter, cuddliness). Short and very short versions exist; (13) The Early Childhood Behavior Questionnaire (ECBQ) serves the same purpose as the IBQ-R, but in young children aged 18 and 36 months. It

ECBQ assesses 18 dimensions of temperament (e.g. attentional focus, cuddliness, discomfort, frustration, impulsivity, shyness); (14) The Child Behavior Checklist (CBCL) 1½ -5 is an assessment of general problem behaviors in preschool children. The information is obtained from parents or teachers using items on eight syndrome scales (emotionally reactive; anxious/depressed; somatic complaints; withdrawn; sleep problems, attention problems; rule-breaking behavior; aggressive behavior). For comprehensive references see “Supplementary Materials”.

Results

A detailed description of adaptations available for each of the reviewed scales or tests per country / linguistic region is provided in the supplementary tables and references (Suppl. Tables 1-14 & references): ADOS in Supplementary Table 1, ADI-R in Supplementary Table 2, SCQ in Supplementary Table 3, SRS in Supplementary Table 4, DAWBA in Supplementary Table 5, Q-CHAT and M-CHAT/-R in Supplementary Table 6, RBS-R in Supplementary Table 7, CDI in Supplementary Table 8, Mullen Scales of Early Learning in Supplementary Table 9, VABS in Supplementary Table 10, ITSP in Supplementary Table 11, IBQ-R in Supplementary Table 12, ECBQ in Supplementary Table 13, and CBCL 1½ -5 in Supplementary Table 14.

A substantial variation was identified in the availability of diagnostic instruments for different countries, cultures, or languages (Table 1), with only three regions (UK/Ireland, Scandinavia, and Belgium/The Netherlands) having access to sufficiently usable forms of all of the 14 diagnostic instruments. Additionally, clinicians and researchers from Israel and Portugal have access to 13 out of 14 proposed diagnostic instruments. For four of the surveyed countries (Romania, Hungary, FYR Macedonia and Czech Republic) less than half of the instruments have been translated or adapted.

About here: Table 1

Not surprisingly, the number of instruments being available per country from a commercial publisher or directly from the authors of the respective tool in an organized fashion (e.g. download from a website) (here called ‘formal distribution’) also varied for different languages and countries/regions. In addition, although many of the available diagnostic tools are also distributed formally, in most cases, the number of available tools is higher than the number of tools distributed formally. The exceptions are UK/Ireland, German speaking countries (Germany, Austria, and Switzerland), Spain, Iceland, and Romania in which all available tools are even distributed formally.

Generally, many of the available (and published) diagnostic instruments have not been specifically standardized for the different European languages and countries/regions (Table 1). Even in the regions with high availability of diagnostic instruments, country/language specific reliability and validity properties or norms/cut-offs are sparse (e.g. in France, Italy, Spain) or missing (e.g. in Israel, Portugal, Finland). German and English speaking countries are exceptions from this observation, even though in the UK and Ireland for some tools there is a high reliance on generalizability of studies from the USA. If one assumes generalizability across English speaking countries, the USA, UK, and Ireland are characterized by the highest number of available, formally distributed as well as normalized methods. Dutch speaking countries as well as Scandinavian countries are other examples of regions with relatively high availability of some usable forms of the diagnostic instruments, which are mostly formally distributed. Country/language specific normalization is, however, less common in case of these regions. Scientists and clinicians from German speaking countries can formally access 11 of the proposed diagnostic instruments, for which two thirds have a culture/language specific standardization. In the case of other regions, even if translated diagnostic instruments

are (formally or informally) available, specific standardizations are lacking. Clinicians and scientists from Czech Republic have the most limited access to diagnostic tools for early ASD assessment. Only 4 out of 14 tools have been translated to Czech, out of which two are formally available but none language specific data has been collected.

About here: Table 2

Table 2 shows the availability of each of the early ASD diagnostic instruments within the totality of European languages/cultural regions. The only widely available tool across Europe is the ADOS/ADOS-2, which is accessible across all the examined language/culture regions. The ADI-R, CBCL, M-CHAT/Q-CHAT and SCQ are available in the majority of regions. Nevertheless, there are not very many publications on these relatively well accessible methods originating in Europe (see Suppl Tables 1-14 & references). Two instruments are particularly infrequently available in Europe: The Mullen Scales of Early Learning and the RBS-R (both available in 4 languages/culture regions). Among the formally distributed tools available in different language versions from commercial publishers are the ADOS-2 and ADI-R. The process of getting both of these published is protracted and takes several years. Instruments formally distributed by their authors are the DAWBA, M-CHAT, and MacArthur-Bates Communicative Development Inventory. Instruments with poor distribution are the ITSP, RBS-R and Mullen Scales of Early Learning. Region/language specific standardizations are scarce or missing for many of the early ASD diagnostic instruments. This holds true even for tools with greater availability. The CDI can be partially considered an exception because it is available in 13 out of 16 examined regions and it has specific norms for 7 of the countries.

Discussion

Psychiatric research is based on reliable phenotyping, predominantly ensured by psychodiagnostic tools including first choice diagnostic instruments (“gold standard”) to determine psychiatric status, general psychopathology or psychological characteristics (e.g. neuropsychological functions, IQ). Nevertheless, many of these scales and tests are only available in a limited number of languages, and have been normalized and validated for an even smaller number of cultural backgrounds. This study examined the (in-)equalities of research prerequisites across Europe regarding the access to diagnostic instruments enabling internationally competitive research on early ASD identification. Our study suggests that the middle-income countries are disadvantaged in Europe. The two included middle-income European countries (Romania, FYR Macedonia) had limited access to diagnostic scales compared to high-income European countries. In addition, limited access to certain instruments was identified in other east European countries (Czech Republic, Hungary, Poland) as well as Iceland, a country with a small population and its own language. However, even in these countries the access to a smaller selection of ASD specific scales, such as the ADOS-2, ADI-R, SCQ or M-CHAT/Q-CHAT or instruments used frequently in international research and practice to evaluate general psychopathology (CBCL) was satisfactory. These scales are either formally distributed by commercial publishers or freely and systematically made available by the authors. A further, less recognized issue in this context is the level of availability of each instrument to clinicians as well the availability of adequate clinical and research training. In many countries where certain tools are not formally distributed, they have been adapted for research purposes only. This means that each administration is subject to license fees paid directly to the copyright holder and in result the instrument is not available for clinical practice. Thus tool availability is further impounded by the need to negotiate license agreements with the publisher of the original version, while the publisher

often sets a number of limitations on the use of data collected with this instrument. This is a particularly sensitive issue in the face of increasing demands for free access to research data put forward by public research funding bodies. As the purpose of this mapping was to examine if European countries can adhere to internationally competitive research protocols (www.eu-aims.eu; www.eurosibs.eu), not the usage of ASD diagnostics in European clinical practice, we did not examine frequencies of usage of the various instruments in relation to either commercial or free distribution. We are therefore unable to evaluate which of the two is generally more beneficial for accessibility and usage. The latter is surely a limitation of the current study, and deserves more attention in future research. It is of paramount interest to the EU-AIMS project mentioned earlier, and strategies and actions to solve related obstacles in Europe have been recently described (Ashwood, Buitelaar, Murphy, Spooren, & Charman, 2014). Still, as commercially distributed instruments are associated with costs for purchase, which are often high for LAMI countries, and entail stricter rules for copyright and terms of usage, free access is probably more advisable to reduce inequalities of research prerequisites concerning instrument access. However, even free access might not solve other challenges for LAMI countries, such as limited access to (expensive) training to ensure quality control of administration, scoring and interpretation, like currently required for the ADOS-2 and ADI-R.

Strikingly, we found that for all European languages/cultural regions, no matter high or middle income, small or large population and rare or frequently spoken language, there was a substantial deficiency of adequate language/cultural standardization. The only language for which standardization was sufficient across instruments was English (UK/Ireland), but only when assuming high intercultural validity between these countries and USA. Most scales originate from the USA, and generalizability of psychometric properties and norms to high income European countries is often assumed. However, several studies, for instance those from Germany or Sweden on the ADOS-2, ADI-R or SRS show that this is only partially true

(Bölte & Poustka, 2004; Bölte, Poustka, & Constantino, 2008; Zander et al., 2014). The latter demonstrates the need for increased cross-cultural research in the field of psychometric evaluation, an extremely and continuously underfunded area of science. This is unfortunate, as a large part of psychiatric research of all kind is based on reliable phenotyping, predominantly ensured by psychodiagnostic tools.

Reasons for international research imbalances in terms of tool availability and other aspects are multifaceted. Proximal causes include the fact that the amount of research conducted in LAMI countries is comparably small and more likely to be of lower scientific quality than in high-income countries (Alem & Kebede, 2003). There are extremely few research skilled psychiatrists, clinical psychologists and other mental health professionals, and those who are, mostly work clinically, with a strong need to focus on health care services. Researchers face difficult circumstances in LAMI countries, owing to social, political and economic situations that do not or cannot prioritize psychiatry research, leading to a lack of funding, poor equipment, and inadequate education. Moreover, a low level of scientific culture with no research and publication tradition hampers research (Jablensky, 1999). Our study also points out research disadvantages in developed countries with small populations and rarely spoken languages (e.g. Iceland). This is an obvious challenge, but it has rarely been discussed previously in the literature.

The underrepresentation of certain countries, especially LAMI countries in psychiatry research is both ethically and scientifically challenging. Ethically, The World Mental Health report has pointed-out the immense burden of psychiatric problems and disability that are associated with mental disorders in LAMI countries (Desjarlais, 1996), and the research gap also reflects the well-known 10/90 global divide: less than 10% of the world's research resources are earmarked for more than 90% of the health problems (*The 10/90 report on health research 2000*). Scientifically, it is reasonable to support the use of the research

capacities and findings from LAMI countries. Their inclusion might reduce research and publication bias, by providing a lot broader perspective on mental health and possibly new significant insights into basic and applied psychiatry. To a lesser degree this might even be true for developed countries, with small populations or rarely spoken languages.

To increase underrepresented countries, collaborative research between LAMI and more scientifically established countries is fruitful (Doku & Mallett, 2003). Several international collaborations have previously raised awareness for inequalities in psychological and psychiatric research prerequisites including the availability of scales to assess child development. For instance, The World Psychiatric Association (WPA) Task Force, initiated activities aiming to support psychiatry journals (e.g. with PubMed indexation) in LAMI countries (de Jesus Mari et al., 2009), the Grand Challenges in Global Mental Health initiative by the US National Institute of Mental Health has identified research priorities to impact on mental health internationally (Collins et al., 2011), The WHO-launched collaborative longitudinal study of schizophrenia (Padma, 2014), and the Grand Challenges in Global Mental Health initiatives (Collins et al., 2011) aim to disclose overseen obstacles for international psychiatric research. In terms of diagnostic tool availability, The Etiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) cohort study (Murray-Kolb et al., 2014). Across 8 sites, in Bangladesh, Brazil, India, Nepal, Pakistan, Peru, South Africa, and Tanzania, the Bayley Scales of Infant and Toddler Development and a modified MacArthur Communicative Development Inventory were adapted. Herein, the authors explicitly point-out the complexity and costs of worldwide psychodiagnostic tool harmonization, in order to raise awareness among funders for future research support in this area of science.

The current mapping study is the first to review lacking diagnostic scale availability in early assessment of childhood ASD for research purposes from a cross-national perspective.

Initiatives such as COST-ESSEA, and outcomes from these initiatives, such as the present study, can help to generate awareness of research inequalities in ASD and other neurodevelopmental disorders. They might serve as a decision pad for policy makers and the international research community to overcome those inequalities. Future studies in the area should investigate the status quo of tool availability in ASD beyond Europe, also include scales for adolescent and adult ASD, and also incorporate research prerequisites in relation clinical practice.

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Table 1. Total number of assessment tools (out of 14 examined in this review) available in each of the 16 language/cultural groups.

Region	Availability	Standardization	Formal distribution
UK, Ireland	14	9 (1)*	14
Scandinavia	14	5	13
Belgium, The Netherlands	14	7	12
Israel	13	0	11
Portugal	13	0	8
France	12	3	11
Finland	12	0	11
Germany, Austria, Switzerland	11	8	11
Italy	11	3	9
Spain	11	4	11
Poland	9	1	8
Iceland	8	1	8
Romania	6	0	6
Hungary	6	0	5
Macedonia	5	1	3
Czech Republic	4	0	2

Note. Column “availability” summarizes the total number of assessment tools for which a language version exists; column “standardization” shows how many of those language specific versions have country specific psychometrics; column “formal distribution” contains information regarding the number of psychological assessment tools which are formally distributed (by a publisher or the authors of the method) per language/cultural group

* Number in brackets indicates the number of assessment tools with UK, Ireland standardization (other value includes USA specific normalizations).

Table 2. Availability of each of the assessment tools per language/culture groups.

	Availability	Standardization	Formal distribution
<i>ADOS</i>	16	3	14
<i>ADI-R</i>	15	4	13
<i>CBCL</i>	15	3	14
<i>CHAT</i>	14	3	12
<i>SCQ</i>	14	2	13
<i>CDI</i>	13	7	13
<i>DAWBA</i>	13	1	13
<i>VABS</i>	12	4	11
<i>IBQ-R</i>	12	3	12
<i>ECBQ-R</i>	11	0	11
<i>SRS</i>	11	3	8
<i>ITSP</i>	9	1	5
<i>RBS-R</i>	4	0	1
<i>MSEL</i>	4	0	3

Note. ASD-specific scales are marked with bold italics. Column “availability” indicates the number of language/culture groups for which a given method is available; column “standardization” specifies in how many of the assessed language/culture groups the diagnostic instrument has been specifically standardized; column “formal distribution” specifies in how many of the assessed language/culture groups the diagnostic instrument is formally distributed (by a publisher or the authors of the method).

ADOS = Autism Diagnostic Observation Schedule, ADI-R = Autism Diagnostic Interview-Revised, CBCL = Child Behavior Checklist, CHAT = Modified Checklist for Autism in Toddlers, SCQ = Social Communication Questionnaire, CDI = McArthur-Bates Communicative Development Inventory, DAWBA = Development and Well-Being Assessment, VABS = Vineland Adaptive Behavior Scales, IBQ-R = Infant Behavior Questionnaire – Revised, ECBQ-R = Early Childhood Behavior Questionnaire, SRS = Social Responsiveness Scale, ITSP = Infant Toddler Sensory Profile, RBS-R = Repetitive Behavior Scale – Revised, MSEL = Mullen Scales of Early Learning.

Supplementary Material (ESM)

[Click here to download Supplementary Material \(ESM\): aut_COST_ScaleMapp_Suppl Tables 1-14 & references_final_01_2015.docx](#)